either 0.15 or 0.3 ug/ml, and then analyzed by flow cytometry. B cells were identified by gating on cells positive for the lineage marker CD19). CpG ODN 2006 was a strong inducer of B cell proliferation, and this effect was reduced if the CpG motifs were methylated or inverted to GpC as shown in Figures 1A, B, C and D at an ODN concentration of 0.3 ug/ml. The base composition of the ODN appears to be important in determining the immune stimulatory effect. Reducing the T content of an ODN substantially reduces immune stimulatory effect, as exemplified by ODN 2177 (SEQ ID NO. 427) in which 6 of the Ts present in ODN 2137 (SEQ ID NO. 886) have been switched to A's, resulting in a greatly reduced immune stimulatory effect. The importance of T's in the immune stimulatory effect of an ODN is also shown by comparison of ODN 2116 (SEQ ID NO. 357) and 2181 (SEQ ID NO. 431), which differ in the 3' end of the ODN. ODN 2181, in which the 3' end is poly-T is more stimulatory than ODN 2116, in which the 3' end is poly-C, despite the fact that both ODN have a TCGTCG at the 5' end.

B2 cont

Remarks

The amendments to the specification were warranted in view of the preparation of the formal drawings (herewith submitted). Figure 1A, as originally filed, is now labeled as Figure 1A and Figure 1B; and Figure 1B, as originally filed, is now labeled as Figure 1C and Figure 1D.

Under "Brief Description of the Drawings" Applicants have now inserted a description of Figures 1B and 1D. The description of these figures would be obvious in view of the originally filed figures. Accordingly, no new matter has been added.

Respectfully Submitted,

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APPENDIX A

MARKED-UP SPECIFICATION

Please amend the specification paragraphs as indicated below:.

Please amend the two paragraphs beginning on page 22, lines 24, as follows:

Figure 1A is a histogram of the expression of CD86 (Y-axis) by CD19+ cells following exposure of these cells to the oligonucleotides shown on the X-axis at a concentration of 0.15 μg/ml.

Figure 1B is a table with the data from Figure 1A.

Figure 1[B]C is a histogram of the expression of CD86 (Y-axis) by CD19+ cells following exposure of these cells to the oligonucleotides shown on the X-axis at a concentration of 0.30 μg/ml.

Figure 1D is a table with the data from Figure 1C.

Please amend the paragraph beginning on page 130, line 7, as follows:

To assess the ability of T-rich ODN to activate B cell proliferation, human PBMCs were stained with the cytoplasmic dye CSFE, incubated with five days with the indicated ODN at either 0.15 or 0.3 ug/ml, and then analyzed by flow cytometry. B cells were identified by gating on cells positive for the lineage marker CD19). CpG ODN 2006 was a strong inducer of B cell proliferation, and this effect was reduced if the CpG motifs were methylated or inverted to GpC as shown in Figures 1A, B, C and D at an ODN concentration of 0.3 ug/ml. The base composition of the ODN appears to be important in determining the immune stimulatory effect. Reducing the T content of an ODN substantially reduces immune stimulatory effect, as exemplified by ODN 2177 (SEQ ID NO. 427) in which 6 of the Ts present in ODN 2137 (SEQ ID NO. 886) have been switched to A's, resulting in a greatly reduced immune stimulatory effect. The importance of T's in the immune stimulatory effect of an ODN is also shown by comparison of ODN 2116 (SEQ ID NO. 357) and 2181 (SEQ ID NO. 431), which differ in the 3' end of the ODN. ODN 2181, in which the 3' end is poly-T is more stimulatory than ODN 2116, in which the 3' end is poly-C, despite the fact that both ODN have a TCGTCG at the 5' end.